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Antiangiogenesis treatment for gliomas: transfer of antisense-vascular endothelial growth factor inhibits tumor growth in vivo.

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Presently, there is no effective treatment for glioblastoma, the most malignant and common brain tumor. Angiogenic factors are potentially optimal targets for therapeutic strategies because they are essential for tumor growth and progression. In this study, we sought a strategy for efficiently delivering an antisense cDNA molecule of the vascular endothelial growth factor (VEGF) to glioma cells. The recombinant adenoviral vector Ad5CMV-alphaVEGF carried the coding sequence of wild-type VEGF165 cDNA in an antisense orientation. Infection of U-87 MG malignant glioma cells with the Ad5CMV-alphaVEGF resulted in reduction of the level of the endogenous VEGF mRNA and drastically decreased the production of the targeted secretory form of the VEGF protein. Treatment of s.c. human glioma tumors established in nude mice with intralesional injection of Ad5CMV-alphaVEGF inhibited tumor growth. Taken together, these findings indicate that the efficient down-regulation of the VEGF produced by tumoral cells using antisense strategies has an antitumor effect in vivo. This is the first time that an adenoviral vector is used to transfer antisense VEGF sequence into glioma cells in an animal model, and our results suggest that this system may have clinical and therapeutic utility.

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